



BACKGROUND INFORMATION FOR THE MEDIA

Polymerase Chain Reaction (PCR) Testing

Polymerase chain reaction (PCR) testing is a method of assessing whether a patient has achieved and is maintaining a molecular response – the disappearance or reduction in quantities of Bcr-Abl, which produces the abnormal protein responsible for proliferation of white blood cells that occurs in chronic myeloid leukaemia patients - via the measurement of Bcr-Abl transcripts

Biology of Chronic Myeloid Leukemia (CML)

CML is a haematologic malignancy in which white blood cells do not mature and become too numerous. It is characterised by the presence of an abnormality called the Philadelphia (Ph) chromosome, detected in the bone marrow of approximately 95% of patients with CML. This is the hallmark of the disease.

At the time of diagnosis, CML patients typically have a significantly elevated white blood cell count. Once CML has been diagnosed further testing defines the stage / extent of the disease to help develop a treatment plan. Three primary stages are:

- Chronic phase
- Accelerated phase
- Blast phase

The primary goal of therapy is the elimination of the Ph chromosome from the bone marrow – considered a complete cytogenetic response (CCR).

Criteria for measuring efficacy of CML treatment

Once CML is diagnosed, further testing defines the stage or extent of disease and helps in developing a treatment plan. The stages of CML include:

Haematologic response – A complete haematologic response refers to the normalisation of blood counts, which last for at least four weeks, effectively identifying the degree to which the most apparent abnormality in CML (i.e. proliferation of white blood cells) is controlled. During a haematologic response, the Ph chromosome-positive (Ph+) cells may still be present

Cytogenetic response – A cytogenetic response, traditionally regarded by researchers as compelling evidence that a particular treatment is effective, is the disappearance or reduction of the number of Ph+ cells detectable by standard lab methods. This indicates the degree to which the underlying cause of the disease itself is controlled

Molecular response – Bcr-Abl transcripts can still be in evidence even when cytogenetic response is attained. While attaining cytogenetic response is important, many researchers suggest that the best outcomes may be achieved when patients with CML demonstrate a molecular response (MR). In CML, a molecular response is the disappearance or reduction in quantities of Bcr-Abl, which produces the abnormal protein responsible for proliferation of white blood cells that occurs in CML patients. A complete molecular response (CMR) indicates that Bcr-Abl levels are undetectable. MR has been found to correlate with both cytogenetic response and progression-free survival.^{1,2}

PCR testing

The best way to assess whether a patient has achieved and is maintaining a molecular response is via a relatively new technique - “real-time” quantitative polymerase chain reaction (RQ-PCR) testing.³ PCR testing can measure even minute levels of Bcr-Abl transcripts.

Because patients treated with the small molecule targeting therapy imatinib (Glivec[®]) as first-line therapy tend to achieve high overall rates of complete haematologic and cytogenetic response,⁴ the degree of Glivec efficacy has been further examined by measuring trace levels of Bcr-Abl transcripts in patients who achieved a complete cytogenetic response.

PCR testing is available at certified laboratories. PCR tests are based on standardised molecular monitoring and reporting standards, enabling the physician access to consistent and easily interpretable PCR results. However, currently PCR monitoring is not widespread and results can differ considerably between labs, making interpretation and practical application difficult.

PCR testing and the European Treatment and Outcome Study (EUTOS) for CML

The European LeukemiaNet (ELN) and Novartis have established the European Treatment and Outcome Study (EUTOS) for CML, an initiative designed to help European healthcare professionals to optimize treatment and achieve the best possible outcomes for patients with CML. EUTOS for CML will offer healthcare professionals a comprehensive clinical support program, including access to the latest disease management tools and techniques to help further improve treatment outcomes for patients with CML.

A key initiative of will be to expand access to state of the art clinical support programs; including PCR testing in certified European laboratories with significant expertise in PCR and using a standardised methodology developed by a consensus of international experts.

ENDS

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References:

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